Faulty gene linked to condition in infants

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(Medical Xpress)—Researchers at King's College London have for the first time identified a defective gene at the root of Vici syndrome, a rare inherited disorder which affects infants from birth, leading to impaired development of the brain, eyes and skin, and progressive failure of the heart, skeletal muscles and the immune system.

Published in the journal *Nature Genetics*, the study identified a defect in the EPG-5 gene, indicating a genetic cause of the condition which was previously unknown. Researchers at King's and Guy's & St Thomas' NHS Foundation Trust, part of King's Health Partners, analysed the DNA of 18 infants with Vici syndrome and identified the inactivity of EPG-5 as a major cause of the condition.

Infants born with Vici syndrome inherit two copies of the defective gene, one from each parent. Although there are only around 50 known cases of the disorder across the world, researchers believe the precise

incidence is unknown due to lack of awareness of this condition. Dr Heinz Jungbluth, from the Children's Neuroscience Centre at St Thomas' Hospital, who led the study along with Professor Mathias Gautel from the Cardiovascular Division at King's, said: 'Vici syndrome is likely to be under-diagnosed as there is potential for misdiagnosis, particularly when you consider the many different organ systems affected by Vici and the significant overlap with other, more common disorders.'

The study also highlighted the 'autophagy' process and the role of EPG-5 in causing this mechanism to fail. Autophagy is a highly regulated cellular process that removes damaged or unwanted components, which is crucial for the health of all cell types, including those involved in muscles, the immune system and brain development. Abnormalities in this process have been implicated previously in neurodegenerative conditions, but defects causing disorders of normal development such as Vici syndrome have rarely been reported. The researchers suggest that autophagy could play a key role in causing a range of disorders, offering the potential for treatment of other conditions. Dr Jungbluth said: 'Although the condition is very rare, it is likely that insights provided by research into Vici syndrome will also be transferable to the diagnosis and therapy of neurodegenerative and neurodevelopmental disorders, and a wider range of primary muscle conditions.'

Professor Gautel added: 'Having identified where this genetic defect occurs we are now able to explore potential interventions. For instance, there is the possibility of enhancing other pathways unaffected by the EPG-5 gene, or by preventing use of the defective pathway in the first place.'

As the defective gene is inherited from both the mother and father, there is also the possibility of screening families with a known history of Vici syndrome. Professor Gautel said: 'Mothers could be offered preimplantation diagnosis, which involves removing a cell from an

embryo when it is around three days old and testing it for genetic disorders, so that an unaffected embryo can be implanted into the mother's womb, if necessary.'

More information: www.nature.com/ng/journal/vaop … nt/full/ng.2497.html

Provided by King's College London